

Early Tacrolimus Concentrations Are Influenced by Genetic and Clinical Factors in Chinese Lung Transplant Patients

Du W¹, Wang X¹, Zhang D¹, Chen W¹, Wang X¹, Zhang X¹, Chen W², Li P¹

¹ Department of Pharmacy, China-Japan Friendship Hospital, Beijing, China;

² Department of Lung Transplantation, China-Japan Friendship Hospital, Beijing, China

Background The 2019 Therapeutic Drug Monitoring (TDM) consensus report on tacrolimus proposed using *CYP3A5**3 and *CYP3A4**22 to guide its initial dosing. However, this dosing strategy does not seem applicable for Chinese patients since *CYP3A4**22 allele is absent in Asians. Apart from pharmacogenomic (PG) factors, clinical factors may also account for residual variability in tacrolimus pharmacokinetics (PK). Therefore, we aim to investigate potential PG and clinical factors on tacrolimus concentration in Chinese lung transplant patients in the early post-operative period. **Methods** 80 Chinese lung transplant patients who had undergone lung transplantation and were treated with tacrolimus from August 2017 to February 2019 were included in this retrospective study. For genetic factors, we included *CYP3A5**3, *CYP3A4**1G, *ABCB1* (3435T>C) and *POR**28. Clinical factors were obtained from patients' electronic medical records. The trough concentration/dose normalized by body weight (C_0/D) ratios were calculated for the first 3 weeks after transplantation. **Results** Among 4 SNPs investigated in our study, only *CYP3A5**3 was associated with tacrolimus C_0/D . In clinical factors, voriconazole use showed positive correlation with C_0/D . A model with PG and clinical factors explained 63.3%, 59.6% and 65.9% of concentration variance in the first 3 weeks respectively compared with 46.6%, 16.9% and 8.8% for *CYP3A5**3 only. When patients using voriconazole were excluded, *CYP3A5**3 accounted for 54.9%, 31.1% and 20.2% variations in tacrolimus concentration in the first 3 weeks. **Conclusions** In early post-operative period, *CYP3A5**3 and usage of voriconazole were the main influential genetic factor affecting tacrolimus C_0/D . When relying concentration to adjust tacrolimus dosing, incorporating both genetic and clinical factors may be an optimal choice.

Key Words: tacrolimus, voriconazole, *CYP3A5*, lung transplant